SHORT REPORTS

Effect of dual chamber pacing on raised plasma atrial natriuretic peptide concentrations in complete atrioventricular block

Atrial natriuretic peptide is released into the circulation in normal humans in situations of increased central blood volume and hence atrial pressure, such as head out immersion in water.[1] The same stimulus of raised atrial pressure is also responsible for the increased plasma concentrations of atrial natriuretic peptide observed in pathological states of fluid overload, including cardiac and renal failure.[2] Raised atrial pressures also occur in patients with complete atrioventricular block because of the frequent occurrence of atrial systole during ventricular systole. In theory this could provide an adequate stimulus for a sustained rise in plasma atrial natriuretic peptide concentrations. Dual chamber pacing restores the normal sequence of atrial and ventricular contraction, whereas ventricular pacing leaves atrial and ventricular systole uncoordinated. We used these pacing modes to determine the relative effects on plasma atrial natriuretic peptide concentration of coordinated and dissociated atrial and ventricular chamber contraction.

Patients, methods, and results

Thirty two patients (17 men and 15 women, aged 44-85) with complete atrioventricular block were studied. All had normal atrial activity and none had retrograde atrioventricular conduction, cardiac failure, or renal failure. Six of these patients (aged 72 (SEM 14)), who presented acutely with complete atrioventricular block, had a dual chamber mode programmable pacemaker implanted. Plasma atrial natriuretic peptide concentrations (determined by radioimmunoassay[3]) were measured before pacing and at the end of each of two consecutive 30 day periods. During these periods patients were paced in ventricular demand mode at 70 beats/min and in dual chamber mode (back up 70 beats/min, upper rate 125-150 beats/min, and atrioventricular delay of 150 ms) in randomised order. Plasma atrial natriuretic peptide concentration was also estimated in 13 patients (aged 71 (2), atrial rate 78 (2) beats/min) paced in ventricular demand mode at 70 beats/min for 43 (6) months and in 13 patients (aged 63 (4), atrial rate 72 (3) beats/min) paced in dual chamber mode (programmed as above) for 40 (4) months. Thirteen of the patients were paced with ventricular demand pacing rather than the preferred dual chamber mode, either because dual chamber pacing had not yet become available (seven patients) or because of disease in other systems (six patients). Atrial natriuretic peptide values were compared with those from 13 age and sex matched convalescent hospital patients with no cardiac or renal disease.

The mean plasma atrial natriuretic peptide concentration in patients presenting with complete atrioventricular block was 141 (28) pmol/l compared with 58 (7) pmol/l in the controls. These raised concentrations were essentially unchanged after ventricular demand pacing for 30 days, whereas pacing in dual chamber mode for 30 days returned plasma atrial natriuretic peptide values to normal values (table). In the two groups long term ventricular demand pacing was again associated with raised plasma atrial natriuretic peptide concentrations whereas those paced in dual chamber mode had normal plasma concentrations.

Comment

The frequent simultaneous occurrence of atrial and ventricular systoles in complete atrioventricular block causes episodic raised atrial pressure, which can be observed clinically as cannon waves in the jugular venous pulse.[4] We tested, and confirmed, the hypothesis that these raised atrial pressures increase plasma atrial natriuretic peptide concentrations.

Plasma atrial natriuretic peptide concentration is also raised during paroxysmal tachycardia.[5] The stimulus for atrial natriuretic peptide secretion during these episodes might be either increased atrial pressure or increased heart rate. The occurrence of raised plasma concentrations of atrial natriuretic peptide in the presence of reduced heart rate in complete atrioventricular block suggests, however, that heart rate or even atrial rate per se is not an important independent factor promoting atrial natriuretic peptide secretion. Atrial natriuretic peptide possesses natriuretic and vasodilator properties and also inhibits renin and aldosterone release. Its secretion in conditions of volume overload is therefore clearly appropriate. In complete atrioventricular block, which in these patients was not accompanied by fluid overload, raised plasma atrial natriuretic peptide concentrations may protect against the development of overt cardiac failure.

Dual chamber pacing restores the normal atrioventricular sequence, whereas ventricular demand pacing does not. The restoration of plasma atrial natriuretic peptide concentrations to control values by dual chamber pacing serves to emphasise the physiological nature of this mode.

Plasma atrial natriuretic peptide (ANP) concentrations in controls, patients with complete atrioventricular block unpaced and paced acutely in ventricular demand and dual chamber modes, and patients paced long term in ventricular demand and dual chamber modes

		Study group (n=6)				
	Controls (n=13)	Unpaced	Short term ventricular demand pacing	Short term dual chamber pacing	Long term ventricular demand pacing (n=13)	Long term dual chamber pacing (n=13)
ANP (pmol/l)	58 (7)	141 (28)*	139 (30)	53 (7)	112 (13)**	43 (7)

*p<0·05; **p<0·01 compared with controls (unpaired *t* tests).

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Early diagnosis of chronic fetal hypoxia in a diabetic pregnancy

Late intrauterine fetal death continues to be a problem in diabetic women, and studies of cord blood have implicated hypoxia as a possible cause.[1] The fact that these deaths may occur without warning has led to the practice of early delivery. We describe a diabetic pregnancy in which hypoxia was suspected from Doppler studies of blood velocity in the fetus and was confirmed by cordocentesis.[2]

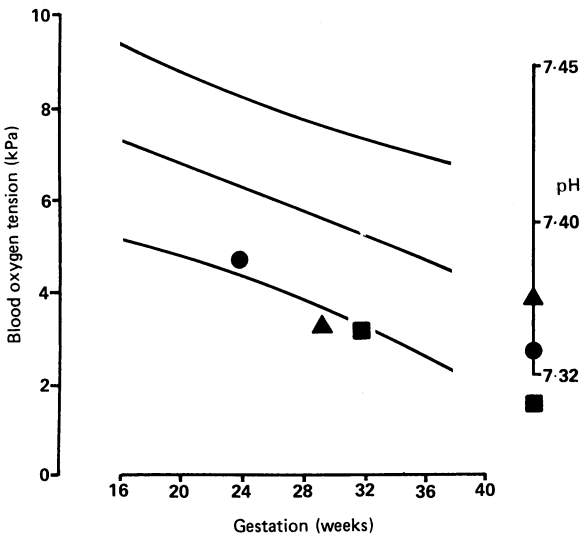
Case report

A 27 year old primigravid, insulin dependent diabetic (White class B) was found to have a high resistance index in the uteroplacental circulation (>95th centile for our normal range) on routine Doppler screening at 23 weeks' gestation. As she had already requested cordocentesis for fetal karyotyping the fetal blood gas tensions were also measured and compared with our normal range[3]: oxygen tension was 4·9 kPa and pH 7·33 (figure). Fetal growth was normal, with a good volume of amniotic fluid. A series of blood glucose tests performed by the mother showed good control of her diabetes, but her glycosylated haemoglobin concentration was raised (mean 13%; range 9·4-17·2%) throughout pregnancy.

At 29 weeks' gestation the Doppler studies showed no end diastolic frequencies in the umbilical artery. Because of the association between this characteristic and hypoxia[4] cordocentesis was repeated. Blood gas tensions confirmed that the fetus was hypoxic but not acidotic (oxygen tension 3·4 kPa, pH 7·35).

Daily inpatient monitoring by Doppler measurement of fetal blood flow showed persistent abnormalities, although cardiotocograms showed reactivity, fetal activity was good, and fetal growth was within the normal range. At 31 weeks

and 5 days' gestation considerable spontaneous decelerations in the fetal heart rate were noted. Further analysis of cord blood showed the fetus to be acidotic (pH 7·31) and hypoxic (oxygen tension 3·3 kPa), and a 1660 g female infant was delivered by caesarean section. The infant required intubation at birth (Apgar scores were three at one minute, seven at five minutes; cord blood pH 7·20) and was transferred to the neonatal intensive care unit. No complications occurred during the postnatal period, and the baby was discharged after 22 days.



Oxygen tension and corresponding pH in cord blood plotted against normal ranges (mean and 95% confidence intervals) during gestation.

Comment

The traditional assessments of fetal growth and activity did not show hypoxia whereas the routine Doppler studies of blood flow allowed the condition to be identified and hence allowed the fetus to be delivered successfully before death could occur. Interestingly, fetal growth recorded by ultrasonography continued normally; abnormalities in blood flow and chronic fetal hypoxia are usually associated with fetuses that are small for gestational age.[5] Owing to the suboptimal control of diabetes in the mother, as shown by the high concentrations of glycosylated haemoglobin, the fetus might have been expected to exceed the average birth weight for gestational age. Most infants born to our diabetic patients (79%) weigh more than the 50th centile. The birth weight of this infant was still on the 35th centile despite chronic hypoxia in utero, suggesting that, although the infant was of an appropriate weight for gestation, she was growth retarded and the accelerating effects of maternal diabetes on growth had been counterbalanced by "placental insufficiency."

Analysis of fetal blood gas tensions at the time of delivery suggested that some infants of diabetic mothers are fairly hypoxic.[1] We recently showed by cordocentesis that the blood oxygen tension of such infants in utero is much lower than normal, providing an explanation for previously "unexplained" late fetal death. Doppler studies of blood flow and cordocentesis may allow fetal hypoxia to be detected earlier than the traditional tests of fetal wellbeing.

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Lactose absorption and milk drinking habits in Estonians with myocardial infarction

In 1980 Segall suggested that a diet rich in lactose might be a risk factor for ischaemic heart disease.[1] Data from 29 different ethnic groups were compared, and a correlation was found between mortality from myocardial infarction on the one hand and efficient lactose absorption in adults and the consumption of milk on the other. Consumption of large quantities of milk is facilitated by high intestinal lactase activity, which is an inherited characteristic.[2]

We undertook a case-control study to test whether the consumption of large quantities of milk and the unhindered absorption of lactose increase the risk of myocardial infarction. The incidence of myocardial infarction in Estonia is one of the highest in the Soviet Union, and the prevalence of primary adult type lactose malabsorption is 24-32%.[2]

Subjects, methods, and results

We studied 70 Estonian men aged 36-78 who were admitted to hospital with acute myocardial infarction. A male patient was matched to each case for age, nationality, and place of residence (urban/rural). These controls had no ischaemic heart disease but were in hospital because of trauma or otorhinolaryngological disease. Informed consent was obtained from each patient. Lactose absorption was determined by a standard 50 g lactose load four weeks later. When the rise in blood glucose concentration was less than 1·1 mmol/l the patient was considered to have lactose malabsorption. There were no cases of general malabsorption as shown by a glucose-galactose load. All the subjects were asked what their average daily regular consumption of fresh milk (200 ml glasses) had been before they became ill.

We used the χ^2 test to calculate the significance of the difference in milk consumption and the prevalence of lactose malabsorption between the two groups. The relative risk of myocardial infarction was expressed by odds ratios comparing differences between the case-control pairs whose consumption of milk differed.[3] Several potentially confounding factors (hypertension, family history of ischaemic heart disease, cigarette smoking, and overweight) were also considered in multiple logistic regression models. Corresponding odds ratios and 95% confidence intervals were calculated from the coefficients and their standard errors.[3,4]

The regular milk consumption in men who had had a myocardial infarction exceeded that of their controls (table; $\chi^2=14·80$, $p<0·01$). The relative risk of myocardial infarction in those drinking three glasses of milk or more daily was four times that of those who drank less than three glasses. When adjusted for potential confounding factors the estimated relative risk for drinking three glasses of milk or more compared with drinking less than three glasses daily was 1·7 ($p<0·05$).

Association between milk drinking and myocardial infarction

Regular milk consumption (No of glasses daily)	Men with myocardial infarction (n=70)	Control subjects (n=70)	Estimated odds ratio (95% confidence interval)
<3	38	59	1·0*
≥3	32	11	4·0 (1·4 to 13·3) 1·7† (1·1 to 2·6)†

*Reference value.
†Figures adjusted to allow for confounding variables.

Twelve of the patients with myocardial infarction and 22 of the controls had lactose malabsorption ($\chi^2=3·88$, $p<0·05$). The estimated relative risk for lactose absorbers and malabsorbers was not significantly different from 1·0.

Comment

Although lactose malabsorption was less common in the patients than the controls, the calculated relative risk failed to show a significant association between myocardial infarction and lactose absorption. Drinking milk in large quantities, however, significantly increased the risk of infarction. The risk associated with milk drinking was independent of hypertension, overweight, cigarette smoking, and a family history of ischaemic heart disease.

Lactose absorption does not seem to be a risk factor for myocardial infarction by itself but is a precondition for the ability to drink a lot of milk without getting complaints. With that proviso our results support the hypothesis that there is an association between ischaemic heart disease and milk intake.[1]